



Consiglio Nazionale delle Ricerche



Malaria breakthrough. A collaboration between ISS, IRBM and CNR has led to the discovery of new molecules blocking the transmission of the parasite.

June 8th 2022, Rome Italy: The Istituto Superiore di Sanità, IRBM and CNR today announced collaborative research published in the journal *Communications Biology* (doi: 10.1038/s42003-022-03510-w) that identified new molecules which block the transmission of the malaria parasite from an infected person to the mosquito, the first step in developing new drugs to eliminate this major infectious disease.

In response to the guidance of the World Health Organization to attack the malaria parasite on multiple fronts, researchers have collaborated, in recent years, in the search for new molecules able to block the transmission of the most dangerous of malarial parasites, *Plasmodium falciparum* - a project funded by the public-private consortium CNCCS, formed by CNR, ISS and IRBM.

This work identified seven molecular structures (chemotypes), three of which have never been identified in the past, able to kill gametocytes and prevent the development of the parasite in the mosquito.

The success of this work was possible thanks to the combination of biological knowledge on the parasite stages transmissible to the *Anopheles* mosquito (the gametocytes), innovative cell-based assays on transgenic parasites and the expertise in large-scale screening of pharmacologically active compounds.

Giacomo Paonessa, Group Leader at IRBM, outlined that "the biological assay funnel developed in this collaboration was able to efficiently and quickly screen 120,000 compounds, which corresponds to about a third of those tested so far by various laboratories all over the world in the search for new parasite anti-transmission drugs. This result therefore paves the way to wider screens to identify even better compounds against parasite transmission. "

"The action of the identified chemotypes is to interrupt the life cycle of *P. falciparum* and therefore the spread of malaria to other individuals" comments Pietro Alano, researcher at ISS, adding that "the advantage of the new screening funnel is its efficiency and speed in identifying molecules active specifically against gametocytes as well as dual active molecules, that are able to kill the parasite stages



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causing the disease symptoms. Today, elimination of malaria requires both types of drugs.”

In the past five years the global fight against malaria has come to a halt, exacerbated today by the effects of the Covid-19 pandemic on the health systems of the most affected countries, mainly in Africa. In 2021, 240 million new cases and 630,000 deaths, especially African children under the age of 5, was the price imposed by this parasite on the health of humanity, a scenario made increasingly worrying by the emergence of parasites and mosquitoes resistant to the available frontline drugs and insecticides.

Istituto Superiore di Sanità (**ISS**), is the main centre for research, control and technical-scientific advice on public health in Italy. It is supervised by the Ministry of Health.

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CNR - National Research Council, is a national research public institution with multidisciplinary proficiency, supervised by the Ministry of Education, University and Research (MUR). Founded in 1923, it has the task of carrying out scientific research projects in the main fields of knowledge, applying their results for the development of the Country, in order to promote innovation, internationalization of the “research system” and fostering the competitiveness of the industrial system.

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The **CNCCS** - National Consortium is a private-public consortium between CNR – Consiglio Nazionale di Ricerca, ISS – Istituto Superiore di Sanità, and IRBM, with a mission to identify compounds acting on innovative biological targets. It also acts as a centre for translational research in rare, neglected and poverty-related diseases. Is a public-private central repository of organic compounds with an associated high throughput screening hub for the identification of novel lead compounds acting on biological targets of interest with the purpose of enabling and accelerating the translation of new basic research discoveries and scientific knowledge into the development of molecules to study gene function and biological mechanisms, and of novel medicines.

IRBM is a drug hunting company working across all aspects of drug discovery and early development for different modalities – small molecule, peptides, and antibodies. IRBM fosters collaborations with organizations from the pharmaceutical, biotech and academic sectors to accelerate drug discovery from target validation and hit identification to candidate nomination.

IRBM's scientists have discovered several drugs that are on the market, and more than 25 compounds have gone into clinical testing.

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